WEST Search History

DATE: Wednesday, September 03, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=ADJ			
L4	L2 and diabet$3	0	L4
L3	L2 and diabetes	0	L3
L2	L1 and sulodexide	5	L2
L1	((514/54 |514/57 |514/62)!.CCLS. |(536/18.7 |536/21 |536/55 |536/55.1 |536/55.2 |536/123.1 |536/123.12)!.CCLS.)	3670	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 14:57:13 ON 03 SEP 2003)

FILE 'CAPLUS, MEDLINE, USPATFULL, AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, ...' ENTERED AT 14:57:30 ON 03 SEP 2003

L1 31373 S DIABETIC NEPHROPATHY
L2 85 S L1 AND SULODEXIDE
L3 19 S L2 AND ORAL?

L3 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:493637 CAPLUS
DOCUMENT NUMBER: 137:72975
TITLE: **Oral sulodexide** reduces albuminuria in microalbuminuric and macroalbuminuric type 1 and type 2 diabetic patients: the Di.N.A.S. randomized trial
AUTHOR(S): Gambaro, Giovanni; Kinalska, Ida; Oksa, Adrian; Pont'uch, Peter; Hertlova, Miluse; Olsovsky, Jindrich; Manitius, Jacek; Fedele, Domenico; Czekalski, Stanislaw; Perusicova, Jindriska; Skrha, Jan; Taton, Jan; Grzeszczak, Wladyslaw; Crepaldi, Gaetano
CORPORATE SOURCE: Department of Medical and Surgical Science, Division of Nephrology, University of Padua, Padua, Italy
SOURCE: Journal of the American Society of Nephrology (2002), 13(6), 1615-1625
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Diabetic nephropathy** may be effectively prevented and treated by controlling glycemia and administering angiotensin-converting enzyme (ACE) inhibitors. However, strict metabolic control can be difficult, and ACE inhibitors may be poorly tolerated and only partially effective, particularly in diabetes mellitus type 2 (DM2), warranting the search for ancillary treatment. **Sulodexide** is a glycosaminoglycan, a new class of drug that has demonstrated nephroprotective activity in exptl. investigations. The Di.N.A.S. study was a randomized, double-blind, placebo-controlled, multicenter, dose-range finding trial to evaluate the extent and duration of the hypoalbuminuric effect of **oral sulodexide** in diabetic patients. A total of 223 microalbuminuric and macroalbuminuric DM1 and DM2 patients with serum creatinine .ltoreq.150 .mu.mol/L and stable BP and metabolic control were recruited. They were randomly allocated to one of four groups: 50 mg/d, 100 mg/d, or 200 mg/d **sulodexide** daily or placebo for 4 mo (T0 to T4), with 4 mo of follow-up after drug suspension (T4 to T8). Treatment with 200 mg/d **sulodexide** for 4 mo significantly reduced log albumin excretion rate (logAER) from 5.25.+-.0.18 at T0 to 3.98.+-.0.11 at T4 ($P < 0.05$), which was maintained till T8 (4.11.+-.0.13; $P < 0.05$ vs. T0). Moreover, the **sulodexide** -induced percent redns. in AER at T4 were significantly different from the placebo value at T4 and approx. linear to dose increments 30% [confidence limits, 4 to 49%], $P = 0.03$; 49% [30 to 63%], $P = 0.0001$; and 74% [64 to 81 %], $P = 0.0001$ in the **sulodexide** 50, 100, and 200 mg/d groups, resp. At T8, the **sulodexide** 200 mg/d group maintained a 62% (45 to 73%) AER significant redn. vs. placebo ($P = 0.0001$). Subanal. by type of diabetes (DM1 vs. DM2, microalbuminuric vs. macroalbuminuric, or on concomitant ACE inhibitors vs. not on ACE inhibitors) demonstrated similar findings. These effects were obtained without any significant variation in metabolic control and BP or serum creatinine. Very few adverse events were reported; none were serious. In conclusion, a 4-mo course of high doses of **sulodexide** significantly and dose-dependently improves albuminuria in DM1 and DM2 patients and micro- or macroalbuminuric patients with or without concomitant ACE inhibition. The effect on albuminuria is long-lasting and seemingly additive to the ACE inhibitory effect.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:903822 CAPLUS
DOCUMENT NUMBER: 136:25121
TITLE: Compositions containing **sulodexide** for the treatment of **diabetic nephropathy**

INVENTOR(S): Palazzini, Ernesto; Gambaro, Giovanni
PATENT ASSIGNEE(S): Alfa Wassermann, Inc., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001093850	A2	20011213	WO 2001-US18411	20010606
WO 2001093850	A3	20020822		
WO 2001093850	B1	20030220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002065233	A1	20020530	US 2001-873234	20010604
EP 1292315	A2	20030319	EP 2001-939923	20010606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011464	A	20030506	BR 2001-11464	20010606
NO 2002005849	A	20021205	NO 2002-5849	20021205

PRIORITY APPLN. INFO.: US 2000-209907P P 20000607
WO 2001-US18411 W 20010606

AB The present invention provides **oral** formulations of **sulodexide** for the treatment of **diabetic nephropathy** in patients with both insulin dependent and non-insulin dependent diabetes mellitus. **Oral** formulations contg. doses adapted for administration to obtain a redn. in albumin excretion in patients with both micro and macro albuminuria and to produce lasting improvement in albumin excretion rate are provided. Methods of treating **diabetic nephropathy** using these formulations are also provided. The percent redn. in the albumin excretion rate after a 4-mo treatment with **sulodexide** was significantly different from placebo, and approx. linear to dose increments. The group receiving **sulodexide** at 50 mg/day had a 31% redn. in AER.

L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:781013 CAPLUS
DOCUMENT NUMBER: 128:213127
TITLE: Effect of glycosaminoglycans on urinary albumin excretion in insulin-dependent diabetic patients with micro- or macroalbuminuria
AUTHOR(S): Poplawska, A.; Szelachowska, M.; Topolska, J.; Wysocka-Solowie, B.; Kinalska, I.
CORPORATE SOURCE: 24a M. Curie-Sklodowskiej St, Department of Endocrinology, Medical Academy Bialystok, 15-276 Bialystok, Pol.
SOURCE: Diabetes Research and Clinical Practice (1997), 38(2), 109-114
CODEN: DRCPE9; ISSN: 0168-8227
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim here was to investigate whether **sulodexide** treatment is capable of influencing urinary albumin excretion rate (UAER) in insulin-dependent diabetes mellitus patients (type I) with micro- or

macroalbuminuria. A total of 14-inpatients (7 with micro and 7 with macroalbuminuria) were enrolled and were treated first i.m. with a 60 mg vial of **sulodexide**/day for 10 days, and then **orally** with 25 mg capsules twice a day for 21 days. UAER was estd. before starting treatment (T0), after the i.m. treatment phase (T1), and at the end of the **oral** treatment (T2). No differences in hematochem. and coagulative parameters were registered after treatment, with respect to basal values. On the contrary, a marked decrease in UAER mean values was registered at the end of both the parenteral and the **oral** treatment periods (T0: 349.9 mg/24 h, range 80-820; T1: 237 mg/24 h, range 7-620; T2: 91.4 mg/24 h, range: 2-306). All the differences were statistically significant vs. baseline. At T2, a normalization of UAER was obsd. in 3 microalbuminuric and in 2 macroalbuminuric patients, and a remarkable decrease was found in addnl. 4 and 5 patients, resp. UAER was still lower than at baseline after 6 wk of follow-up. This preliminary study suggests that **sulodexide** is effective in reducing UAER in type I patients with **diabetic nephropathy**.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:257956 CAPLUS
DOCUMENT NUMBER: 122:23851
TITLE: Use of **sulodexide** and of medicines containing it for the treatment of **diabetic nephropathy**.
INVENTOR(S): Marchi, Egidio; Tamagnone, Gianfranco
PATENT ASSIGNEE(S): Alfa Wassermann S.p.A., Italy
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 624374	A1	19941117	EP 1994-107051	19940505
EP 624374	B1	20001227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2120062	AA	19941111	CA 1994-2120062	19940328
US 5496807	A	19960305	US 1994-227502	19940414
JP 06329541	A2	19941129	JP 1994-91713	19940428
JP 2702400	B2	19980121		
AT 198278	E	20010115	AT 1994-107051	19940505
ES 2152272	T3	20010201	ES 1994-107051	19940505

PRIORITY APPLN. INFO.: IT 1993-BO205 A 19930510

AB The use of **sulodexide**, a glycosaminoglycan of natural origin extd. from mammalian intestinal mucosa, and of medicines contg. it, in the treatment of patients suffering from nephropathy of diabetic origin is disclosed. The effectiveness of **sulodexide** has been shown by the significant decrease of the albuminuria in microalbuminuric and macroalbuminuric diabetic patients treated with pharmaceutical compns. (**oral** or i.m.) contg. therapeutically effective amts. of the drug.

L3 ANSWER 5 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2002309473 MEDLINE
DOCUMENT NUMBER: 22035508 PubMed ID: 12039991
TITLE: **Oral sulodexide** reduces albuminuria in microalbuminuric and macroalbuminuric type 1 and type 2 diabetic patients: the Di.N.A.S. randomized trial.
AUTHOR: Gambaro Giovanni; Kinalska Ida; Oksa Adrian; Pont'uch Peter; Hertlova Miluse; Olsovsky Jindrich; Manitius Jacek; Fedele Domenico; Czekalski Stanislaw; Perusicova Jindriska;

Skrha Jan; Taton Jan; Grzeszczak Wladyslaw; Crepaldi Gaetano

CORPORATE SOURCE: Department of Medical and Surgical Science, Division of Nephrology, University of Padua, Padua, Italy.. giga@unipd.it

SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (2002 Jun) 13 (6) 1615-25.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020611
Last Updated on STN: 20021211
Entered Medline: 20021104

AB **Diabetic nephropathy** may be effectively prevented and treated by controlling glycemia and administering angiotensin-converting enzyme (ACE) inhibitors. However, strict metabolic control can be difficult, and ACE inhibitors may be poorly tolerated and only partially effective, particularly in diabetes mellitus type 2 (DM2), warranting the search for ancillary treatment. **Sulodexide** is a glycosaminoglycan, a new class of drug that has demonstrated nephroprotective activity in experimental investigations. The Di.N.A.S. study was a randomized, double-blind, placebo-controlled, multicenter, dose-range finding trial to evaluate the extent and duration of the hypoalbuminuric effect of **oral sulodexide** in diabetic patients. A total of 223 microalbuminuric and macroalbuminuric DM1 and DM2 patients with serum creatinine < or =150 micromol/L and stable BP and metabolic control were recruited. They were randomly allocated to one of four groups: 50 mg/d, 100 mg/d, or 200 mg/d **sulodexide** daily or placebo for 4 mo (T0 to T4), with 4 mo of follow-up after drug suspension (T4 to T8). Treatment with 200 mg/d **sulodexide** for 4 mo significantly reduced log albumin excretion rate (logAER) from 5.25 +/- 0.18 at T0 to 3.98 +/- 0.11 at T4 ($P < 0.05$), which was maintained till T8 (4.11 +/- 0.13; $P < 0.05$ versus T0). Moreover, the **sulodexide** -induced percent reductions in AER at T4 were significantly different from the placebo value at T4 and approximately linear to dose increments (30% [confidence limits, 4 to 49%], $P = 0.03$; 49% [30 to 63%], $P = 0.0001$; and 74% [64 to 81%], $P = 0.0001$ in the **sulodexide** 50, 100, and 200 mg/d groups, respectively. At T8, the **sulodexide** 200 mg/d group maintained a 62% (45 to 73%) AER significant reduction versus placebo ($P = 0.0001$). Subanalysis by type of diabetes (DM1 versus DM2, microalbuminuric versus macroalbuminuric, or on concomitant ACE inhibitors versus not on ACE inhibitors) demonstrated similar findings. These effects were obtained without any significant variation in metabolic control and BP or serum creatinine. Very few adverse events were reported; none were serious. In conclusion, a 4-mo course of high doses of **sulodexide** significantly and dose-dependently improves albuminuria in DM1 and DM2 patients and micro- or macroalbuminuric patients with or without concomitant ACE inhibition. The effect on albuminuria is long-lasting and seemingly additive to the ACE inhibitory effect.

L3 ANSWER 6 OF 19 MEDLINE on STN

ACCESSION NUMBER: 2000109387 MEDLINE
DOCUMENT NUMBER: 20109387 PubMed ID: 10645038

TITLE: [The effect of glycosaminoglycan **sulodexide** on albuminuria in patients with diabetes mellitus]. Ucinok glykozaminoglykanu sulodexidu na albuminuriu u pacientov s diabetes mellitus.

AUTHOR: Oksa A; Pontuch P; Kratochvilova H
CORPORATE SOURCE: Department of Pharmacotherapy, Institute of Clinical and Preventive Medicine, Bratislava, Slovakia.. oksa@upkm.sk
SOURCE: BRATISLAVSKE LEKARSKE LISTY, (1999 Sep) 100 (9) 486-9.
Journal code: 0065324. ISSN: 0006-9248.
PUB. COUNTRY: Slovakia
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Slovak
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000210

AB BACKGROUND: Experimental and clinical studies showed a decrease in albuminuria, a marker of **diabetic nephropathy** after administration of heparin or other glycosaminoglycans (GAG). OBJECTIVES: To study the effect of **sulodexide** on albumin excretion rate (AER) in patients with type 1 or type 2 diabetes mellitus (DM). METHODS: Twenty patients (12 of type 1 DM) aged 33-63 yrs (median 45) with microalbuminuria (AER 20-200 micrograms/min) or macroalbuminuria (AER > 200 micrograms/min) were enrolled in open study and received **sulodexide** 60 mg/day i.m. for 3 weeks with further 6-week follow-up without treatment. In the 2nd phase, **sulodexide** 100 mg/day was given p.o. for 8 weeks with further 8-weeks follow-up. Albuminuria in overnight urine samples was analyzed by the RIA method and results (medians with lower and upper quartiles) were compared by the Wilcoxon test. RESULTS: In the 1st phase, AER (microgram/min) decreased from 167 (54-378) at baseline to 118 (78-220) at week 1 ($p < 0.05$), 105 (68-341) at week 2 ($p < 0.05$), and to 114 (56-354) at week 3 (NS). After stopping the treatment, AER gradually raised to baseline values. During the **oral** phase, AER decreased from 253 (37-961) to 137 (35-323) after 1 month ($p < 0.05$) and to 144 (47-588) after 2 months (NS). This effect was prolonged for further 2 months after treatment withdrawal (AER 110 (65-363) micrograms/min, $p < 0.05$). In both phases, the decrease in AER was shown only in patients with macroalbuminuria, but not in those with microalbuminuria. Blood pressure, glomerular filtration rate and metabolic compensation of DM were not changed. CONCLUSION: A short-term treatment with **sulodexide** i.m. or p.o. significantly decreased albuminuria in DM patients. This effect was prolonged for further 2 months after **oral** administration. Therefore, **sulodexide** could be useful in the treatment of **diabetic nephropathy** . (Tab. 3, Ref. 20.)

L3 ANSWER 7 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1998144368 MEDLINE
DOCUMENT NUMBER: 98144368 PubMed ID: 9483374
TITLE: Effect of glycosaminoglycans on urinary albumin excretion in insulin-dependent diabetic patients with micro- or macroalbuminuria.
AUTHOR: Poplawska A; Szelachowska M; Topolska J; Wysocka-Solowie B; Kinalska I
CORPORATE SOURCE: Department of Endocrinology, Medical Academy Bialystok, Poland.
SOURCE: DIABETES RESEARCH AND CLINICAL PRACTICE, (1997 Nov) 38 (2) 109-14.
Journal code: 8508335. ISSN: 0168-8227.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980430

Last Updated on STN: 19980430
Entered Medline: 19980417

AB The aim of this study was to investigate whether **sulodexide** treatment is capable of influencing urinary albumin excretion rate (UAER) in insulin-dependent diabetes mellitus patients (type I) with micro- or macroalbuminuria. A total of 14-inpatients (seven with micro and seven with macroalbuminuria) were enrolled and were treated first intramuscularly with a 60 mg vial of **sulodexide**/day for 10 days, and then **orally** with 25 mg capsules twice a day for 21 days. UAER was estimated before starting treatment (T0), after the i.m. treatment phase (T1) and at the end of the **oral** treatment (T2). No statistically significant differences in hematochemical and coagulative parameters were registered after treatment, with respect to basal values. On the contrary, a marked decrease in UAER mean values was registered at the end of both the parenteral and the **oral** treatment periods (T0: 349.9 mg/24 h, range 80-820; T1: 237 mg/24 h, range 7-620; T2: 91.4 mg/24 h, range: 2-306). All the differences were statistically significant ($P < 0.001$) versus baseline. At T2, a normalisation of UAER was observed in three microalbuminuric and in two macroalbuminuric patients, and a remarkable decrease was found in additional four and five patients, respectively. UAER was found to be still significantly lower than at baseline after 6 weeks of follow-up. This preliminary study suggests that **sulodexide** is effective in reducing UAER in type I patients with **diabetic nephropathy**.

L3 ANSWER 8 OF 19 MEDLINE on STN
ACCESSION NUMBER: 97281640 MEDLINE
DOCUMENT NUMBER: 97281640 PubMed ID: 9135948
TITLE: Glycosaminoglycans delay the progression of nephropathy in NIDDM.
AUTHOR: Solini A; Vergnani L; Ricci F; Crepaldi G
CORPORATE SOURCE: Department of Internal Medicine, University of Padova, Italy.. flr@ifeuniv.unife.it
SOURCE: DIABETES CARE, (1997 May) 20 (5) 819-23.
Journal code: 7805975. ISSN: 0149-5992.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970724

AB OBJECTIVE: To determine the effect of **oral** administration of glycosaminoglycans on metabolic control and albumin excretion rate (AER) in NIDDM patients with increased urinary albumin excretion. RESEARCH DESIGN AND METHODS: Twelve NIDDM hypertensive patients (age 52 +/- 3 years, HbA1c 7.7 +/- 0.2%) on antihypertensive treatment were enrolled in a double-blind placebo-controlled study, assuming either placebo or **sulodexide** (100 mg/day) for 4 months; at the end of this period, a crossover was performed. We have evaluated routine biochemical parameters plus AER and coagulative function every 2 months. RESULTS: Both plasma fibrinogen (from 4.15 +/- 0.32 to 2.77 +/- 0.47 mmol/l) and AER (from 128.3 +/- 40.6 to 39.6 +/- 11.9 micrograms/min) decreased significantly after treatment with glycosaminoglycans in respect to placebo; moreover, blood pressure control ameliorated, also in the absence of any variation of therapy. CONCLUSIONS: Glycosaminoglycan therapy, likely in association with a satisfactory control of blood pressure values, seems to prevent the progression of **diabetic nephropathy** in NIDDM.

L3 ANSWER 9 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2003:17926 USPATFULL

TITLE: Methods using glycosaminoglycans for the treatment of nephropathy
INVENTOR(S): Laster, Morris, Jerusalem, ISRAEL
Shelach, Noa, Jerusalem, ISRAEL
PATENT ASSIGNEE(S): Keryx (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003013680	A1	20030116
APPLICATION INFO.:	US 2002-170063	A1	20020612 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-298132P	20010612 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method for the treatment of HIV-associated nephropathy by administration of glycosaminoglycans, and in particular, by the administration of **sulodexide**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 19 USPATFULL on STN
ACCESSION NUMBER: 2002:126716 USPATFULL
TITLE: Methods and compositions using **sulodexide** for the treatment of **diabetic nephropathy**
INVENTOR(S): Palazzini, Ernesto, Bologna, ITALY
Gambaro, Giovanni, Scorze (Venezia), ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002065233	A1	20020530
APPLICATION INFO.:	US 2001-873234	A1	20010604 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-209907P	20000607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 593
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides **oral** formulations of **Sulodexide** for the treatment of **diabetic nephropathy** in patients with both insulin dependent and non-insulin dependent diabetes mellitus. **Oral** formulations containing doses adapted for administration to obtain a reduction in albumin excretion in patients with both micro and macro albuminuria and to produce lasting improvement in albumin excretion rate are provided. Methods of treating **diabetic nephropathy** using these formulations are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 19 USPATFULL on STN
ACCESSION NUMBER: 96:19080 USPATFULL
TITLE: Method of treatment of **diabetic nephropathy** by means of **sulodexide** of medicines containing it
INVENTOR(S): Marchi, Egidio, Bologna, Italy
Tamagnone, Gianfranco, Bologna, Italy
PATENT ASSIGNEE(S): Alfa Wassermann S.p.A., Pescara, Italy (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5496807		19960305	
APPLICATION INFO.:	US 1994-227502		19940414	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1993-BO205	19930510

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Goldberg, Jerome D.
LEGAL REPRESENTATIVE: Bucknam and Archer
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 332
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of **sulodexide**, a glycosaminoglycan of natural origin extracted from mammalian intestinal mucosa, and of medicines containing it in the treatment of patients suffering from nephropathy of diabetic origin constitutes the object of the present invention. The effectiveness of **sulodexide** has been shown by the significative decrease of the albuminuria in microalbuminuric and macroalbuminuric diabetic patients treated with pharmaceutical compositions administered by **oral** or intramuscular route containing therapeutically effective amounts of drug.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 12 OF 19 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002-0379654 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): **Oral sulodexide** reduces albuminuria in microalbuminuric and macroalbuminuric type 1 and type 2 diabetic patients : The Di.N.A.S. randomized trial
AUTHOR: GAMBARO Giovanni; KINALSKA Ida; OKSA Adrian; PONT'UCH Peter; HERTLOVA Miluse; OLSOVSKY Jindrich; MANITIUS Jacek; FEDELE Domenico; CZEKALSKI Stanislaw; PERUSICOVA Jindriska; SKRHA Jan; TATON Jan; GRZESZCZAK Wladyslaw; CREPALDI Gaetano
CORPORATE SOURCE: Department of Medical and Surgical Science, Division of Nephrology, University of Padua, Padua, Italy; Department of Endocrinology, Medical Academy, Bialystoc, Poland; Institute of Preventive and Clinical Medicine, Clinical Pharmacology Department, Bratislava, Slovakia; First Internal Clinic of Medicine, Faculty Hospital, Bratislava, Slovakia; Internal Clinic, Faculty Hospital, Brno, Czech Republic; Second Internal Clinic of Medicine, Diabetology Day-Hospital, Brno, Czech Republic; Department of Nephrology, The Ludwik Rydygier Medical University in Bydgoszcz, Bydgoszcz, Poland; Department

of Medical and Surgical Science, Diabetic Center, Geriatric Hospital, University of Padua, Padua, Italy; Department of Nephrology, Medical Academy, Poznan, Poland; Third Department of Internal Medicine, Faculty Policlinic, 1.sup.s.sup.t Faculty of Medicine, Charles University, Prague, Czech Republic; Chair and Department of Internal Diseases and Diabetology, Medical School, Warsaw, Poland; Department and Clinic of Internal Diseases and Diabetology, Silesian School of Medicine, Zabrze, Poland; Department of Medical and Surgical Science, 1.sup.s.sup.t Medical Clinic, University of Padua, Padua, Italy

SOURCE: Journal of the American Society of Nephrology, (2002), 13(6), 1615-1625, 45 refs.
ISSN: 1046-6673
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-26049, 354000108654500220
AN 2002-0379654 PASCAL
CP Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
AB **Diabetic nephropathy** may be effectively prevented and treated by controlling glycemia and administering angiotensinconverting enzyme (ACE) inhibitors. However, strict metabolic control can be difficult, and ACE inhibitors may be poorly tolerated and only partially effective, particularly in diabetes mellitus type 2 (DM2), warranting the search for ancillary treatment. **Sulodexide** is a glycosaminoglycan, a new class of drug that has demonstrated nephroprotective activity in experimental investigations. The Di.N.A.S. study was a randomized, double-blind, placebo-controlled, multicenter, dose-range finding trial to evaluate the extent and duration of the hypoalbuminuric effect of **oral sulodexide** in diabetic patients. A total of 223 microalbuminuric and macroalbuminuric DM I and DM2 patients with serum creatinine <=150 .mu.mol/L and stable BP and metabolic control were recruited. They were randomly allocated to one of four groups: 50 mg/d, 100 mg/d, or 200 mg/d **sulodexide** daily or placebo for 4 mo (TO to T4), with 4 mo of follow-up after drug suspension (T4 to T8). Treatment with 200 mg/d **sulodexide** for 4 mo significantly reduced log albumin excretion rate (logAER) from 5.25 .+-. 0.18 at TO to 3.98 .+-. 0.11 at T4 ($P < 0.05$), which was maintained till T8 (4.11 .+-. 0.13; $P < 0.05$ versus T0). Moreover, the **sulodexide** -induced percent reductions in AER at T4 were significantly different from the placebo value at T4 and approximately linear to dose increments (30% [confidence limits, 4 to 49%], $P = 0.03$; 49% [30 to 63%], $P = 0.0001$; and 74% [64 to 81%], $P = 0.0001$ in the **sulodexide** 50, 100, and 200 mg/d groups, respectively. At T8, the **sulodexide** 200 mg/d group maintained a 62% (45 to 73%) AER significant reduction versus placebo ($P = 0.0001$). Subanalysis by type of diabetes (DM 1 versus DM2, microalbuminuric versus macroalbuminuric, or on concomitant ACE inhibitors versus not on ACE inhibitors) demonstrated similar findings. These effects were obtained without any significant variation in metabolic control and BP or serum creatinine. Very few adverse events were reported; none were serious. In conclusion, a 4-mo course of high doses of **sulodexide** significantly and dose-dependently improves albuminuria in DM1 and DM2 patients and micro- or macroalbuminuric patients with or without concomitant ACE inhibition. The effect on albuminuria is long-lasting and seemingly additive to the ACE inhibitory effect.

L3 ANSWER 13 OF 19 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998-0114265 PASCAL
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reserved.
TITLE (IN ENGLISH): Effect of glycosaminoglycans on urinary albumin excretion in insulin-dependent diabetic patients with micro- or macroalbuminuria
AUTHOR: POPLAWSKA A.; SZELACHOWSKA M.; TOPOLSKA J.; WYSOCKA-SOLOWIE B.; KINALSKA I.
CORPORATE SOURCE: Department of Endocrinology, Medical Academy Bialystock, 24a M. Curie-Sklodowskiej St., 15-276 Bialystock, Poland
SOURCE: Diabetes research and clinical practice, (1997), 38(2), 109-114, 12 refs.
ISSN: 0168-8227 CODEN: DRCPE9
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Netherlands
LANGUAGE: English
AVAILABILITY: INIST-20702, 354000078172900050
AN 1998-0114265 PASCAL
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
AB The aim of this study was to investigate whether **sulodexide** treatment is capable of influencing urinary albumin excretion rate (UAER) in insulin-dependent diabetes mellitus patients (type I) with micro- or macroalbuminuria. A total of 14-inpatients (seven with micro and seven with macroalbuminuria) were enrolled and were treated first intramuscularly with a 60 mg vial of **sulodexide**/day for 10 days, and then **orally** with 25 mg capsules twice a day for 21 days. UAER was estimated before starting treatment (T0), after the i.m. treatment phase (T1) and at the end of the **oral** treatment (T2). No statistically significant differences in hematochemical and coagulative parameters were registered after treatment, with respect to basal values. On the contrary, a marked decrease in UAER mean values was registered at the end of both the parenteral and the **oral** treatment periods (T0: 349.9 mg/24 h, range 80-820; T1: 237 mg/24 h, range 7-620; T2: 91.4 mg/24 h, range: 2-306). All the differences were statistically significant ($P < 0.001$) versus baseline. At T2, a normalisation of UAER was observed in three microalbuminuric and in two macroalbuminuric patients, and a remarkable decrease was found in additional four and five patients, respectively. UAER was found to be still significantly lower than at baseline after 6 weeks of follow-up. This preliminary study suggests that **sulodexide** is effective in reducing UAER in type I patients with **diabetic nephropathy**.

L3 ANSWER 14 OF 19 PROMT COPYRIGHT 2003 Gale Group on STN

ACCESSION NUMBER: 2002:56354 PROMT
TITLE: Keryx Biopharmaceuticals to Initiate Phase II Clinical Trial of KRX-101 for The Treatment of AIDS Related Kidney Disease - HIV Associated Nephropathy (HIVAN); HIVAN is a Life-Threatening Complication of AIDS.
SOURCE: PR Newswire, (29 Jan 2002) pp. NYTU02129012002.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 871
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB CAMBRIDGE, Mass. and JERUSALEM, Israel -- Keryx Biopharmaceuticals, Inc. (Nasdaq: KERX; AIM: KRX) today announced that it has received approval from the South African Medicines Control Council for the initiation of a Phase II clinical trial of Keryx's investigational drug candidate KRX-101 (**sulodexide**) for the treatment of Human Immunodeficiency Virus Associated Nephropathy (HIVAN) in AIDS patients. Keryx intends to initiate this trial next month and expects to have the results within this calendar year.

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L3 ANSWER 15 OF 19 PROMT COPYRIGHT 2003 Gale Group on STN

ACCESSION NUMBER: 2002:32350 PROMT
TITLE: Keryx Biopharmaceuticals Obtains Worldwide Rights to Novel Small Molecules Technology; Allows Conversion of Peptide Drugs Into Small Molecules for **Oral** Administration.
SOURCE: PR Newswire, (16 Jan 2002) pp. NYW05516012002.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 931
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB CAMBRIDGE, Mass. and JERUSALEM -- Keryx Biopharmaceuticals, Inc. (Nasdaq: KERX; AIM: KRX), today announced that it has obtained an exclusive worldwide license to a novel technology known as Small Integrated Building-blocks ("SIB"), for the conversion of peptides and other existing drugs into small molecules that have the potential for **oral** delivery.
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L3 ANSWER 16 OF 19 PROMT COPYRIGHT 2003 Gale Group on STN

ACCESSION NUMBER: 2000:862912 PROMT
TITLE: OTHER NEWS TO NOTE.
SOURCE: BIOWORLD Today, (28 Sep 2000) Vol. 11, No. 188.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1964
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Alkermes Inc., of Cambridge, Mass., completed enrollment in the first clinical trial of its proprietary injectable sustained-release formulation of naltrexone, an FDA-approved drug used for the treatment of alcoholism and opiate abuse. The drug is currently available in a daily **oral** form. Medisorb naltrexone is based on Alkermes' Medisorb injectable sustained-release drug delivery technology. Based on early data, Alkermes is preparing for larger efficacy trials. Data from the trial will be presented at the 39th annual meeting of the American College of Neuropsychopharmacology in December.
THIS IS THE FULL TEXT: COPYRIGHT 2000 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week).

L3 ANSWER 17 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2002:480435 SCISEARCH
THE GENUINE ARTICLE: 557PW
TITLE: **Oral sulodexide** reduces albuminuria in microalbuminuric and macroalbuminuric type I and type 2 diabetic patients: The Di.NAS randomized trial
AUTHOR: Gambaro G (Reprint); Kinalska I; Oksa A; Pont'uch P; Hertlova M; Olsovsky J; Manitius J; Fedele D; Czekalski S; Perusicova J; Skrha J; Taton J; Grzeszczak W; Crepaldi G
CORPORATE SOURCE: Univ Hosp, Div Nephrol, Dept Med & Surg Sci, Via Giustiniani 2, I-35128 Padua, Italy (Reprint); Univ Padua, Div Nephrol, Dept Med & Surg Sci, Padua, Italy; Med Acad Bialystok, Dept Endocrinol, Bialystok, Poland; Inst Prevent & Clin Med, Dept Clin Pharmacol, Bratislava, Slovakia; Fac Hosp, Internal Med Clin 1, Bratislava, Slovakia; Fac Hosp, Internal Clin, Brno, Czech Republic; Diabetol Day Hosp, Dept Internal Clin Med 2, Brno, Czech Republic; Ludwik Rydygier Med Univ Bydgoszez, Dept

Nephrol, Bydgoszcz, Poland; Univ Padua, Geriatr Hosp, Ctr Diabet, Dept Med & Surg Sci, Padua, Italy; Med Acad, Dept Nephrol, Poznan, Poland; Charles Univ, Fac Med 1, Fac Policlin, Dept Internal Med 3, Prague, Czech Republic; Sch Med, Chair & Dept Internal Dis & Diabetol, Warsaw, Poland; L Warynski Silesian Med Acad, Dept & Clin Internal Dis & Diabetol, Zabrze, Poland; Univ Padua, Med Clin 1, Dept Med & Surg Sci, Padua, Italy

COUNTRY OF AUTHOR: Italy; Poland; Slovakia; Czech Republic
SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (JUN 2002) Vol. 13, No. 6, pp. 1615-1625.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.
ISSN: 1046-6673.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Diabetic nephropathy** may be effectively prevented and treated by controlling glycemia and administering angiotensin-converting enzyme (ACE) inhibitors. However, strict metabolic control can be difficult. and ACE inhibitors may be poorly tolerated and only partially effective, particularly in diabetes mellitus type 2 (DM2), warranting the search for ancillary treatment. **Sulodexide** is a glycosaminoglycan, a new class of drug that has demonstrated nephroprotective activity in experimental investigations. The Di.N.A.S. study was a randomized. double-blind, placebo-controlled, multicenter, dose-range finding trial to evaluate the extent and duration of the hypoalbuminuric effect of **oral sulodexide** in diabetic patients. A total of 223 microalbuminuric and macroalbuminuric DM1 and DM2 patients with serum creatinine less than or equal to150 mumol/L and stable BP and metabolic control were recruited. They were randomly allocated to one of four groups: 50 mg/d. 100 mg/d. or 200 mg/d **sulodexide** daily or placebo for 4 mo (T0 to T4), with 4 mo of follow-up after drug suspension (T4 to T8). Treatment with 200 mg/d **sulodexide** for 4 mo significantly reduced log albumin excretion rate (logAER) from 5.25 +/- 0.18 at TO to 3.98 +/- 0.11 at T4 ($P < 0.05$), which was maintained till T8 (14.11 +/- 0.13: $P < 0.05$ versus T0). Moreover, the **sulodexide** -induced percent reductions in AER at T4 were significantly different front the placebo value at T4 and approximately linear to dose increments (30% [confidence limits, 4 to 49%]. $P = 0.03$: 49% [30 to 63%]. $P = 0.0001$: and 74% [64 to 81 %], $P = 0.0001$ in the **sulodexide** 50, 100, and 200 mg/d groups. respectively. At T8, the **sulodexide** 200 mg/d group maintained a 62%, (45 to 73%) AER significant reduction versus placebo ($P = 0.0001$). Subanalysis by type of diabetes (DM1 versus DM2, microalbuminuric versus macroalbuminuric, or on concomitant ACE inhibitors versits not on ACE inhibitors) demonstrated similar findings. These effects were obtained without tiny significant variation in metabolic control and BP or serum creatinine. Very few adverse events were reported; none were serious. In conclusion, a 4-mo course of high doses of **sulodexide** significantly and dose-dependently improves albuminuria in DM1 and DM2 patients and micro- or macroalbuminuric patients with or without concomitant ACE inhibition. The effect on albuminuria is long-lasting and seemingly additive to the ACE inhibitory effect.

L3 ANSWER 18 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

ACCESSION NUMBER: 1998:102873 SCISEARCH
THE GENUINE ARTICLE: YT866

TITLE: Effect of glycosaminoglycans on urinary albumin excretion in insulin-dependent diabetic patients with micro- or macroalbuminuria

AUTHOR: Poplawska A (Reprint); Szelachowska M; Topolska J; WysockaSolowie B; Kinalska I
CORPORATE SOURCE: MED ACAD BIALYSTOK, DEPT ENDOCRINOL, 24A M CURIE

SKLODOWSKIEJ ST, PL-15276 BIALYSTOK, POLAND (Reprint)
COUNTRY OF AUTHOR: POLAND
SOURCE: DIABETES RESEARCH AND CLINICAL PRACTICE, (NOV 1997) Vol. 38, No. 2, pp. 109-114.
Publisher: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND.
ISSN: 0168-8227.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 12

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The aim of this study was to investigate whether **sulodexide** treatment is capable of influencing urinary albumin excretion rate (UAER) in insulin-dependent diabetes mellitus patients (type I) with micro-or macroalbuminuria. A total of 14-inpatients (seven with micro and seven with macroalbuminuria) were enrolled and were treated first intramuscularly with a 60 mg vial of **sulodexide**/day for 10 days, and then **orally** with 25 mg capsules twice a day for 21 days. UAER was estimated before starting treatment (T0), after the i.m. treatment phase (T1) and at the end of the **oral** treatment (T2). No statistically significant differences in hematochemical and coagulative parameters were registered after treatment, with respect to basal values. On the contrary, a marked decrease in UAER mean values was registered at the end of both the parenteral and the **oral** treatment periods (T0: 349.9 mg/24 h, range 80-820; T1: 237 mg/24 h, range 7-620; T2: 91.4 mg/24 h, range: 2-306). All the differences were statistically significant ($P < 0.001$) versus baseline. Al T2, a normalisation of UAER was observed in three microalbuminuric and in two macroalbuminuric patients, and a remarkable decrease was found in additional four and five patients, respectively. UAER was found to be still significantly lower than at baseline after 6 weeks of follow-up. This preliminary study suggests that **sulodexide** is effective in reducing UAER in type I patients with **diabetic nephropathy**. (C) 1997 Elsevier Science Ireland Ltd.

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ACCESSION NUMBER: 97:346999 SCISEARCH
THE GENUINE ARTICLE: WW589
TITLE: Glycosaminoglycans delay the progression of nephropathy in NIDDM
AUTHOR: Solini A (Reprint); Vergnani L; Ricci F; Crepaldi G
CORPORATE SOURCE: UNIV FERRARA, DEPT INTERNAL MED 2, VIA SAVONAROLA 9, I-44100 FERRARA, ITALY (Reprint); UNIV PADUA, DEPT INTERNAL MED, I-35100 PADUA, ITALY
COUNTRY OF AUTHOR: ITALY
SOURCE: DIABETES CARE, (MAY 1997) Vol. 20, No. 5, pp. 819-823.
Publisher: AMER DIABETES ASSOC, 1660 DUKE ST, ALEXANDRIA, VA 22314.
ISSN: 0149-5992.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB OBJECTIVE - To determine the effect of **oral** administration of glycosaminoglycans on metabolic control and albumin excretion rate (AER) in NIDDM patients with increased urinary albumin excretion.

RESEARCH DESIGN AND METHODS - Twelve NIDDM hypertensive patients (age 52 +/- 3 years, HbA(1c) 7.7 +/- 0.2%) on antihypertensive treatment were enrolled in a double-blind placebo-controlled study, assuming either placebo or **sulodexide** (100 mg/day) for 4 months; at the end of this period, a crossover was performed. We have evaluated routine

biochemical parameters plus AER and coagulative function every 2 months.

RESULTS - Both plasma fibrinogen (from 4.15 +/- 0.32 to 2.77 +/- 0.47 mmol/l) and AER (from 128.3 +/- 40.6 to 39.6 +/- 11.9 mu g/min) decreased significantly after treatment with glycosaminoglycans in respect to placebo; moreover, blood pressure control ameliorated, also in the absence of any variation of therapy.

CONCLUSIONS - Glycosaminoglycan therapy, likely in association with a satisfactory control of blood pressure values, seems to prevent the progression of **diabetic nephropathy** in NIDDM.

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